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EXAMINER	
MCGILLEM, LAURA L	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/717,573	WU ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *15-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (claims 1-14) in the reply filed on 3/15/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 15-29 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/15/2006.

Claims 1-14 are under examination.

Drawings

The drawings are objected to because figure 11 is partially illegible. The 4th line of nucleotide sequence is not visible. It addition, the 4th line contains what appears to be a label of nucleotide location (-1944) that is out of order with the rest of the sequence labels along the left of the figure. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must

be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

It appears that Applicants have submitted color photographs and drawings. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Specification

The use of the trademarks LIPOFECTIN, SUPERFECT, TRANFECTAM and QIAGEN (see paragraph 0059, for example) has been noted in this application. They

should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-9 and 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is vague and indefinite because it recites the phrase "isolated from upstream region of zebrafish L-FABP" and it is not clear what is meant by upstream region of L-FABP, since L-FABP is a protein.

Claim 8 recites the limitation "said nucleic acid sequence of SEQ ID NO:1 or a variant thereof". There is insufficient antecedent basis for this limitation in the claim, because claim 8 is dependent on claim 1, and claim 1 does not recite SEQ ID NO:1 or a variant thereof.

Claim 10 recites the limitation "said nucleic acid sequence of SEQ ID NO:1" in line 30. There is insufficient antecedent basis for this limitation in the claim, because

claim 10 is dependent on claim 1, and claim 1 does not recite "nucleic acid sequence of SEQ ID NO:1".

Claim 11 recites the limitation "said nucleic acid sequence of SEQ ID NO:1 " in line 4. There is insufficient antecedent basis for this limitation in the claim, because claim 11 is dependent on claim 1, and claim 1 does not recite "nucleic acid sequence of SEQ ID NO:1".

Claims 12 and 14 are vague and indefinite because they recite the phrase "basal promoter" and the metes and bounds of what constitutes a basal promoter are not clear. The specification equates basal promoter with core promoter, which is disclosed as the proximal region upstream of the L-FABP coding sequences containing several consensus motifs. Therefore, the specification does not disclose a specific definition of what a basal promoter must contain in order to considered a "basal promoter".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim an isolated polynucleotide comprising a liver-specific expression control sequence that modulates expression of a vertebrate liver fatty acid binding protein (L-FABP), which encompasses any polynucleotide with the ability to modulate L-FABP expression. Applicants also claim an isolated polynucleotide that modulates expression of a vertebrate L-FABP comprising a nucleic acid sequence of SEQ ID NO:1 or a variant thereof or a variant thereof having at least 80% homology to the nucleic acid sequence or SEQ ID NO:2 or a variant thereof having at least 80% homology to the nucleic acid sequence or SEQ ID NO:3 or a variant thereof having at least 80% homology to the nucleic acid sequence.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

In the instant case, the specification discloses SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3 for the claimed expression control sequence. SEQ ID NOs:1-3 appear to be overlapping nucleotide sequences in which SEQ ID NO:2 comprises the sequence of SEQ ID NO:1 and SEQ ID NO:3. SEQ ID NO:3 appears to comprise SEQ ID NO:1. The specification discloses that the expression control sequence comprises several binding sites for HFH1, HFH2, HNF-1α, HNF-3β, PDX1 and PDX2. There is no description of mutational sites which naturally occur in the molecule and there is no description of how

the structure of the disclosed SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 relates to the structure of the liver-specific expression control sequence. The genus would be expected to have divergent functional properties as small changes in nucleotide sequence can have significant effects on the structure and properties of binding properties of expression control sequences. The applicant does not provide an indication of how the sequence of SEQ ID NO:1 is representative of other variants of SEQ ID NO:1 or variants having at least 80% homology to SEQ ID NO:1. The applicant does not provide an indication of how the sequence of SEQ ID NO:2 is representative of variants having at least 80% homology to SEQ ID NO:2. The applicant does not provide an indication of how the sequence of SEQ ID NO:3 is representative of variants having at least 80% homology to SEQ ID NO:3. The identifying attributes of a polynucleotide that comprises a liver-specific expression control sequence that has the function of modulation of L-FABP expression are not described. The identifying attributes of the individual variants of SEQ ID NO:1 having at least 80% homology to SEQ ID NO:1 are not described. The identifying attributes of the individual variants of SEQ ID NO:2 having at least 80% homology to SEQ ID NO:2 are not described. The identifying attributes of the individual variants of SEQ ID NO:3 having at least 80% homology to SEQ ID NO:3 are not described. For example, variants of SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 having at least 80% (82%, 84%, 86%, 88%, 90% or 95%, etc.) homology to SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 have not been sufficiently described so that one of skill in the art would know that each has the function of modulating expression of a vertebrate L-FABP.

With regard to those claims that embrace any molecule having a recited function, an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property, i.e. modulation of expression of a vertebrate L-FABP, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variant of the genus and is insufficient to support them.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhong et al (Genomics, 1998, Feb 15;48(1):136-8).

Zhong et al teach the construction of a zebrafish genomic library from zebrafish embryos in yeast artificial chromosomes. Zhong et al teach that the mean size of the genomic clones is 470 kb and that the library provides 4.7 fold coverage of the zebrafish genome. Therefore, the zebrafish genomic library taught by Zhong et al would inherently contain a basal promoter of a zebrafish isolated polynucleotide comprising a liver-specific expression control sequence from upstream of a gene for L-FABP wherein said sequence modulates expression of a zebrafish L-FBAP. The zebrafish genomic library would also contain nucleotide sequences comprising binding sites for HFH(1) (SEQ ID NO:4), HFH(2) (SEQ ID NO:5), HNF-1α (SEQ ID NO:6) and HNF-3β (SEQ ID NO:7), as well as nucleotide sequences comprising binding sites for PDX1 (SEQ ID NO:8), and PDX2(SEQ ID NO:9). The zebrafish genomic library would inherently also contain nucleic acid sequences comprising SEQ ID NOs:1, 2 and 3. Claim 12 recites the phrase "linked to a reporter sequence" and does not specify a heterologous reporter sequence. The specification does not disclose a specific definition of reporter sequence.

Since expressed L-FABP would be detectable with a specific antibody or an L-FABP transcription product would be detectable using methods of nucleic acid hybridization, the sequence encoding the L-FABP meets the limitation of a reporter sequence since detection of expressed L-FABP could be used to report promoter activity.

Claims 1-3 and 12-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Her et al (of record).

Claims 1 and 12 do not include the limitation of a specific sequence for the isolated polynucleotide comprising a liver-specific control sequence, wherein the expression control sequence modulates expression of a vertebrate L-FABP.

Her et al teach a 2.8kb liver-specific promoter region from the zebrafish L-FABP gene that was extracted from zebrafish genomic DNA, cloned and ligated into a pEGFP-C1 vector. Her et al teach that the identity of the clone was verified by sequencing, based on L-FABP cDNA (see page 126, left column, 1st paragraph), which reads on an isolated polynucleotide comprising a liver-specific control sequence, wherein the expression control sequence modulates expression of a zebrafish L-FABP. Absent evidence to the contrary, this sequence would modulate expression of a zebrafish L-FABP. Her et al teach that the 5' flanking promoter region of zebrafish L-FABP was cloned into a vector operably linked to GFP and contains all the necessary elements to direct GFP gene expression (see page 125, right column, 1st paragraph and page 126, right column, 5th paragraph), which reads on a recombinant construct comprising a

zebrafish basal promoter and a polynucleotide comprising a liver-specific control sequence operably linked to a GFP reporter sequence.

Claim 1, 6 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Falk et al (U.S. Patent No. 5,625,124).

Claims 6, 10 and 11 recite the phrase "a nucleic acid sequence of" which encompasses any two or more contiguous nucleotides of the claimed sequence. As discussed above, the limitation of the phrase "linked to a reporter sequence" in claim 12 encompasses an expressed protein detectable with a specific antibody or an transcription product detectable using methods of nucleic acid hybridization.

Falk et al teach an expression vector comprising the promoter sequence (nt -596 to +21) of rat liver fatty acid binding protein (Fabpl) linked to the nucleotide sequence encoding human growth hormone (see column 2, lines 57-60, column 6, lines, 22-25, Figure 4 and SEQ ID NO:5, for example), which reads on an isolated polynucleotide comprising a liver-specific expression control sequence wherein said sequence modulates expression of a vertebrate L-FBAP. Absent evidence to the contrary, the polynucleotide sequence taught by Falk et al would modulate expression of a rat Fabpl. The promoter sequence taught by Falk et al comprises two or more contiguous nucleotides of instant SEQ ID NO:1. For example, nt 71 to nt 75 (AAAAA) of SEQ ID NO:5 taught by Falk et al corresponds to nt 274 to nt 278 (AAAAA) of claimed SEQ ID NO:1. The promoter sequence taught by Falk et al comprises two or more contiguous nucleotides of instant SEQ ID NO:2. For example, nt 71 to nt 75 (AAAAA) of SEQ ID

NO:5 taught by Falk et al corresponds to nt 1116 to nt 1120 (AAAAA) of claimed SEQ ID NO:2. The promoter sequence taught by Falk et al comprises two or more contiguous nucleotides of instant SEQ ID NO:3. For example, nt 71 to nt 75 (AAAAA) of SEQ ID NO:5 taught by Falk et al corresponds to nt 363 to nt 367 (AAAAA) of claimed SEQ ID NO:3. The expression vector taught by Falk et al comprising a promoter sequence of Fabpl linked to the nucleotide sequence encoding human growth hormone anticipates the claimed recombinant construct comprising a basal promoter and a reporter sequence wherein the human growth hormone encodes a detectable protein and therefore is a reporter sequence.

Claims 1, 6 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Simon et al (of record).

As discussed above, claims 6, 10 and 11 recite the phrase "a nucleic acid sequence of" which encompasses any two or more contiguous nucleotides of the claimed sequence. Simon et al teach a plasmid construct comprising the 5' non-transcribed domain -1600 to +21bp of rat Fabpl operably linked to a gene encoding human growth hormone (see page 18346, right column and Figure 1, for example). Simon et al teach that this sequence has two potential HNF1 binding sites and a binding site that is very similar to that found for HNF2 (see page 18348, left column, 5th paragraph, for example). Simon et al further teach that a portion of the 5' domain of the Fabpl gene was sufficient to recapitulate developmental intestinal cell expression patterns as seen normally in the rat (see page 18348, right column, last paragraph, bridging to page 18349, left column, in particular). Therefore, the plasmid taught by

Simon et al anticipates an isolated polynucleotide comprising a liver specific expression control sequence that modulates vertebrate liver fatty acid binding protein expression. Simon et al teach a portion of the promoter sequence that comprises a sequence at nt -75 to nt -66 of 5'TGACCTAT**GGG**CCT-3' (page 18348, left column, 5th paragraph, in particular). Instant SEQ ID NO:1 comprises the sequence GGG from nt 233 to nt 235, which corresponds to the GGG sequence taught by Simon et al. Instant SEQ ID NO:2 comprises the sequence GGG from nt 1091 to nt 1093, which corresponds to the GGG sequence taught by Simon et al. Instant SEQ ID NO:3 comprises the sequence GGG from nt 341 to nt 343, which corresponds to the GGG sequence taught by Simon et al. Further, the plasmid construct taught by Simon et al comprising a promoter sequence of Fabpl linked to the nucleotide sequence encoding human growth hormone anticipates the claimed recombinant construct comprising a basal promoter and a reporter sequence wherein the human growth hormone encodes a detectable protein and is therefore a reporter sequence

Claims 1, 12 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Gerard et al (U.S. Patent No. 6,503,498).

Gerard et al teach methods and compositions to express apolipoprotein A-1 in liver cells. Gerard et al teach that a liver-specific promoter for liver fatty acid binding protein would be useful in an adenoviral vector to permit liver-specific expression of apoA-1 in mammals (see column 4, lines 17-30, for example), which reads on an isolated polynucleotide comprising a liver-specific expression control sequence wherein

said sequence modulates expression of a L-FBAP. Absent evidence to the contrary, the polynucleotide sequence taught by Gerard et al would modulate expression of a mammalian L-FBAP. Gerard et al teach the use of CMV, SV40 or RSV promoters with the sequence encoding apoA-1 (see column 9, lines 25-43, for example), which reads on a basal promoter as a CMV, SV40 or RSV promoter. The embodiment of the composition taught by Gerard et al comprising a liver fatty acid binding protein operably linked to apoA-1 comprises a recombinant construct comprising a basal promoter operably linked to a reporter sequence for apoA-1 encodes a detectable protein and is therefore a reporter sequence.

Claims 1, 6, 10 and 11-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Yamanouchi et al (U.S. Patent No. 6,794,154).

Yamanouchi et al teach isolation of the entire human L-FABP coding region including the 5' upstream region from a human chromosomal DNA library, which was then cloned into a reporter plasmid.

The promoter sequence taught by Yamanouchi et al comprises two or more contiguous nucleotides of instant SEQ ID NO:1. For example, nt 638 to nt 641 (AAAA) of SEQ ID NO:1 taught by Yamanouchi et al corresponds to nt 274 to nt 279 (AAAA) of claimed SEQ ID NO:1. The promoter sequence taught by Yamanouchi et al comprises two or more contiguous nucleotides of instant SEQ ID NO:2. For example, nt 638 to nt 641 (AAAA) of SEQ ID NO:1 taught by Yamanouchi et al corresponds to nt 1117 to nt 1120 (AAAAA) of claimed SEQ ID NO:2. The promoter sequence taught by

Yamanouchi et al comprises two or more contiguous nucleotides of instant SEQ ID NO:3. For example, nt 638 to nt 641 (AAAA) of SEQ ID NO:5 taught by Yamanouchi et al corresponds to nt 363 to nt 366 (AAAA) of claimed SEQ ID NO:3. Yamanouchi et al teach that this L-FABP reporter plasmid comprises the 5' upstream region, including the transcriptional regulatory region of human L-FABP and a luciferase gene (see column 8, lines 8-50, in particular), which reads on an isolated polynucleotide comprising a liver-specific expression control sequence wherein said sequence modulates expression of a L-FBAP and a recombinant construct comprising a liver-specific FBAP expression control sequence linked to a reporter sequence

Claims 1, 12 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Hogaboam et al (U.S. Patent No. 6,719,969, filed 8/4/2000).

Hogaboam et al teach compositions to express CXC chemokines in hepatocytes. Hogaboam et al teach that a liver-specific promoter for liver fatty acid binding protein would be useful in an vector to permit liver-specific expression of CXC chemokines in mammals (see column 45, lines 5-10, for example), which reads on an isolated polynucleotide comprising a liver-specific expression control sequence wherein said sequence modulates expression of a L-FBAP. Absent evidence to the contrary, the polynucleotide sequence taught by Hogaboam et al would modulate expression of a mammalian L-FBAP. Hogaboam et al teach the use of CMV, SV40 or RSV promoters with the sequence encoding CXC chemokines (see column 5, lines 56-62, for example), which reads on a basal promoter as a CMV, SV40 or RSV promoter. The embodiment

of the composition taught by Hogaboam et al comprising a liver fatty acid binding protein promoter operably linked to CXC chemokine sequence comprises a recombinant construct comprising a basal promoter operably linked to a reporter sequence for CXC chemokine encodes a detectable protein and is therefore a reporter sequence.

Claims 1, 4-6, 8-9, 12 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. AL929535, submitted 2/7/2003 by Tracey.

As the claim 6 is written, it recites the phrase "a nucleic acid sequence of SEQ ID NO:1" and therefore encompasses nucleic acids that comprise the full-length sequence of SEQ ID NO:1 or any portion of SEQ ID NO:1 including a dinucleotide or larger oligonucleotide.

As claims 4-5 and 8-9 are written, they recite the phrase "having a nucleotide sequence of SEQ ID NO:" 4 or 5 or 6 or 7 or 8 or 9 and therefore encompasses nucleic acids that comprise the full-length sequences of the claimed SEQ ID NOs or any portion of the claimed SEQ ID Nos including a dinucleotide or larger oligonucleotide.

Accession No. AL929535 is a 162435 base pair zebrafish DNA sequence from clone CH211-15101. Accession No. AL929535 has a 46.9% overall sequence identity with SEQ ID NO:1 but between nucleotides (nt) 28,852-29,141, has an 83.8% local similarity with SEQ ID NO:1 from nt 2-289 (see page 10 of Accession No. AL929535 Genbank report). Absent evidence to the contrary, this polynucleotide sequence comprises a liver-specific expression control sequence. Nucleotides 28,852-29,141 of

Accession No. AL929535 read on a nucleic acid sequence of SEQ ID NO:1 or variant thereof having at least 80% homology to SEQ ID NO:1. Accession No. AL929535 comprises a sequence from ~nt 28858 to ~nt 28878 that has high similarity to SEQ ID NO:8, comprises a sequence from ~nt 28885 to ~nt 28904 that has high similarity to SEQ ID NO:9, and comprises a sequence from ~nt 29052 to ~nt 29066 that has high similarity to SEQ ID NO:4. The nucleotide sequence of SEQ ID NO:5 comprises a ggg series of nucleotides, which is identical to nt 29103 to nt 29106 of Accession No. AL929535. The nucleotide sequence of SEQ ID NO:6 comprises a ttt series of nucleotides, which is identical to nt 28914 to nt 28916 of Accession No. AL929535. The nucleotide sequence of SEQ ID NO:7 comprises an aaa series of nucleotides, which is identical to nt 29029 to nt 29031 of Accession No. AL929535. Therefore, the nucleotide sequence of Accession No. AL929535 anticipates an isolated polynucleotide comprising a L-FABP expression control sequence comprising binding sites for HFH(1) having a nucleotide sequence of SEQ ID NO:4, HFH(2) having a nucleotide sequence of SEQ ID NO:5, HNF-1α having a nucleotide sequence of SEQ ID NO:6, and HNF-3β having a nucleotide sequence of SEQ ID NO:7 and comprising binding sites for PDX1 having a nucleotide sequence of SEQ ID NO:8 and/or PDX2 having a nucleotide sequence of SEQ ID NO:9. The nucleotide sequence of Accession No. AL929535 also anticipates an isolated polynucleotide comprising a variant of SEQ ID NO:1 comprising binding sites for HFH(1) having a nucleotide sequence of SEQ ID NO:4, HFH(2) having a nucleotide sequence of SEQ ID NO:5, HNF-1α having a nucleotide sequence of SEQ ID NO:6, and HNF-3β having a nucleotide sequence of SEQ ID NO:7 and comprising binding sites

for PDX1 having a nucleotide sequence of SEQ ID NO:8 and/or PDX2 having a nucleotide sequence of SEQ ID NO:9. Furthermore, the clone CH211-15101 comprising the zebrafish DNA sequence anticipates a recombinant construct comprising a zebrafish basal promoter and a L-FABP expression control sequence operably linked to the L-FABP gene which reads on a reporter sequence.

Claims 1, 4-6, 8-9, 12 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. AC139623, submitted 2/7/2003 by Akhter et al.

Accession No. AC139623 is a *Danio rerio* strain DNA sequence from clone CH211-216G21. Accession No. AC139623 has a 46.5% overall sequence identity with SEQ ID NO:1 but between nt 28,840-29,114, has an 85.8% local similarity with SEQ ID NO:1 from nt 2-275 (see page 11 of Accession No. AC139623 Genbank report). Absent evidence to the contrary, this polynucleotide sequence comprises a liver-specific expression control sequence. Nucleotides 28,840-29,114 of Accession No. AC139623 read on a nucleic acid sequence of SEQ ID NO:1 or variant thereof having at least 80% homology to SEQ ID NO:1.

Accession No. AC1396235 comprises a sequence from ~nt 28846 to ~nt 28867 that has high similarity to SEQ ID NO:8, comprises a sequence from ~nt 28875 to ~nt 28885 that has high similarity to SEQ ID NO:9, and comprises a sequence from ~nt 29041 to ~nt 29055 that has high similarity to SEQ ID NO:4. The nucleotide sequence of SEQ ID NO:5 comprises a ggg series of nucleotides, which is identical to nt 29090 to nt 29093 of Accession No. AC139623. The nucleotide sequence of SEQ ID NO:6

comprises a ttt series of nucleotides, which is identical to nt 28902 to nt 28905 of Accession No. AC139623. The nucleotide sequence of SEQ ID NO:7 comprises an aaa series of nucleotides, which is identical to nt 29016 to nt 29019 of Accession No. AC139623. Therefore, the nucleotide sequence of Accession No. AC139623 anticipates an isolated polynucleotide comprising a L-FABP expression control sequence comprising binding sites for HFH(1) having a nucleotide sequence of SEQ ID NO:4, HFH(2) having a nucleotide sequence of SEQ ID NO:5, HNF-1α having a nucleotide sequence of SEQ ID NO:6, and HNF-3β having a nucleotide sequence of SEQ ID NO:7 and comprising binding sites for PDX1 having a nucleotide sequence of SEQ ID NO:8 and/or PDX2 having a nucleotide sequence of SEQ ID NO:9. The nucleotide sequence of Accession No. AC139623 also anticipates an isolated polynucleotide comprising a variant of SEQ ID NO:1 comprising binding sites for HFH(1) having a nucleotide sequence of SEQ ID NO:4, HFH(2) having a nucleotide sequence of SEQ ID NO:5, HNF-1α having a nucleotide sequence of SEQ ID NO:6, and HNF-3β having a nucleotide sequence of SEQ ID NO:7 and comprising binding sites for PDX1 having a nucleotide sequence of SEQ ID NO:8 and/or PDX2 having a nucleotide sequence of SEQ ID NO:9. Furthermore, the clone CH211-216G21 comprising the zebrafish DNA sequence anticipates a recombinant construct comprising a zebrafish basal promoter and a L-FABP expression control sequence operably linked to the L-FABP gene which reads on a reporter sequence.

Claims 1, 4-6 and 8-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. BX240588, submitted 1/27/2003 by Humphray et al.

Accession No. BX240588 is a present in a *Danio rerio* genomic clone known as DKEY-288B14. Accession No. BX240588 has a 46.9% overall sequence identity with SEQ ID NO:1, but between nt 222-473, has an 90.9% local similarity with SEQ ID NO:1 from nt 2-250 (see Accession No. BX240588 Genbank report). Absent evidence to the contrary, this polynucleotide sequence comprises a liver-specific expression control sequence. Nucleotides 222-473 of Accession No. BX240588 read on a nucleic acid sequence of SEQ ID NO:1 or variant thereof having at least 80% homology to SEQ ID NO:1.

Accession No. BX240588 comprises a sequence from ~nt 465 to ~nt 444 that has high similarity to SEQ ID NO:8, comprises a sequence from ~nt 441 to ~nt 421 that has high similarity to SEQ ID NO:9, and comprises a sequence from ~nt 271 to ~nt 257 that has high similarity to SEQ ID NO:4. The nucleotide sequence of SEQ ID NO:5 comprises a ggg series of nucleotides, which is identical to nt231 to nt 234 of Accession No. BX240588. The nucleotide sequence of SEQ ID NO:6 comprises a ttt series of nucleotides, which is identical to nt 415 to nt 417 of Accession No. BX240588. The nucleotide sequence of SEQ ID NO:7 comprises an aaa series of nucleotides, which is identical to nt 294 to nt 292 of Accession No. AC139623. Therefore, the nucleotide sequence of Accession No. BX240588 anticipates an isolated polynucleotide comprising a L-FABP expression control sequence comprising binding sites for HFH(1) having a nucleotide sequence of SEQ ID NO:4, HFH(2) having a nucleotide sequence

of SEQ ID NO:5, HNF-1α having a nucleotide sequence of SEQ ID NO:6, and HNF-3β having a nucleotide sequence of SEQ ID NO:7 and comprising binding sites for PDX1 having a nucleotide sequence of SEQ ID NO:8 and/or PDX2 having a nucleotide sequence of SEQ ID NO:9. The nucleotide sequence of Accession No. BX240588 also anticipates an isolated polynucleotide comprising a variant of SEQ ID NO:1 comprising binding sites for HFH(1) having a nucleotide sequence of SEQ ID NO:4, HFH(2) having a nucleotide sequence of SEQ ID NO:5, HNF-1α having a nucleotide sequence of SEQ ID NO:6, and HNF-3β having a nucleotide sequence of SEQ ID NO:7 and comprising binding sites for PDX1 having a nucleotide sequence of SEQ ID NO:8 and/or PDX2 having a nucleotide sequence of SEQ ID NO:9.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Laura McGillem, PhD
5/11/2006

DANIEL M. SULLIVAN
PATENT EXAMINER